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Tandem catalysis in ionic liquids: a recyclable catalytic synthesis of benzofuran derivatives

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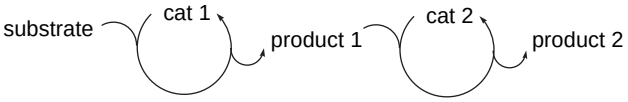
ABSTRACT

A convenient, recyclable catalytic synthesis of benzofuran-2-acetic esters **2** by sequential Pd(0)-catalyzed deallylation—Pd(II)-catalyzed carbonylative heterocyclization of 1-(2-allyloxyphenyl)-2-yn-1-ols **1** in ionic liquids is presented. Reactions were typically carried out in $BmimBF_4$ as the solvent at 100 °C and under 30 atm of CO, in the presence of catalytic amounts (1 mol %) of PdI_2 in conjunction with KI (1 equiv), PPh_3 (4 mol %), MeOH (28 equiv), and H_2O (2 equiv). The solvent-catalyst system could be recycled several times without appreciable loss of catalytic activity.

1. Introduction

Cascade reactions are powerful synthetic tools for constructing functionalized molecules in one step starting from simple and readily available building blocks.[1] In this view, 'sequential' or 'tandem' catalysis, in which the product of a first catalytic cycle becomes the substrate of a second catalytic cycle and so on (Scheme 1), has recently acquired a growing importance in synthesis.[2]



Scheme 1. The concept of 'sequential' or 'tandem' catalysis.

Some years ago, we disclosed a novel approach to benzofuran-2-acetic esters **2** starting from 1-(2-allyloxyphenyl)-2-yn-1-ols **1** through the sequential combination between two catalytic cycles (Scheme 2).[3] The first cycle corresponded to the deprotection of the phenolic oxygen of **1**, while the second process corresponded to a carbonylative heterocyclization process eventually leading to the final benzofuran derivative in high yields and selectivities. For this particular type of tandem catalysis we coined the term 'sequential homobimetallic catalysis', since the two cycles were catalyzed by the same metal, but in two different oxidation states: in particular, the first cycle was catalyzed by a Ph_3P-stabilized Pd(0) species, while the second cycle was catalyzed by a PdI_2-based species (Scheme 2).

Reactions were typically carried out in MeOH as the solvent at 100 °C and under 30–90 atm of CO, in the presence of catalytic amounts of PdI_2 in conjunction with KI, PPh_3, and H_2O. Under these conditions, PdI_2, besides being the catalyst for the second catalytic cycle, also acted as a precursor for the formation in situ of the Pd(0) species promoting the first catalytic cycle, according to Scheme 3.[3]

In this work, we report the results obtained when the tandem catalytic process was carried out in ionic liquids (ILs) as the reaction media, using MeOH as external nucleophile. Ionic liquids are a well established class of non-conventional solvents, characterized by low flammability, low volatility, and low toxicity.[4,5] A very attractive feature of ILs is the possibility to recycle them and to easily recover the product (by simple extraction procedures). Moreover, in the case of catalytic reactions, it may also be possible to recycle the catalyst-solvent system several times, which makes the use of ILs particularly convenient.[4,5]

2. Results and discussion

We have found that the catalytic transformation of 1-(2-allyloxyphenyl)-2-yn-1-ols **1** into benzofurans **2** can be expediently accomplished in an ionic liquid, such as $BmimBF_4$, as the reaction

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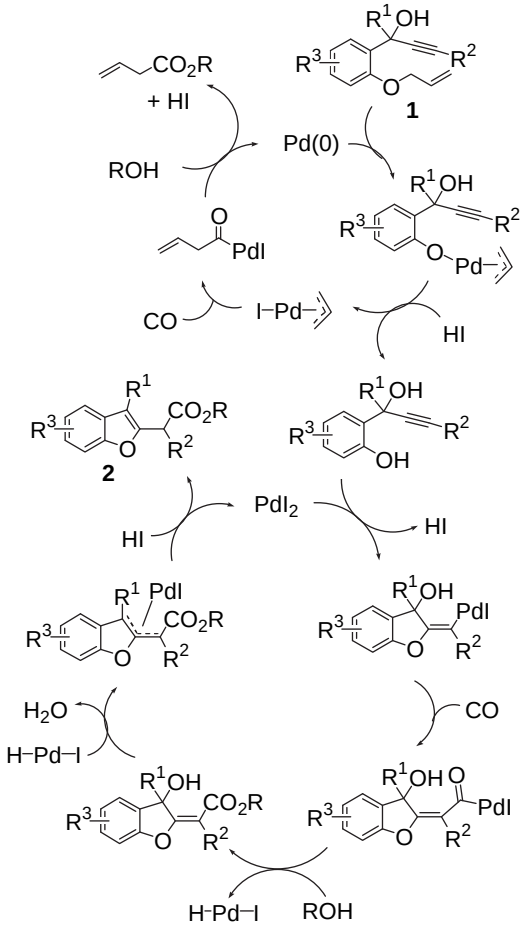
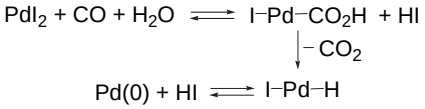
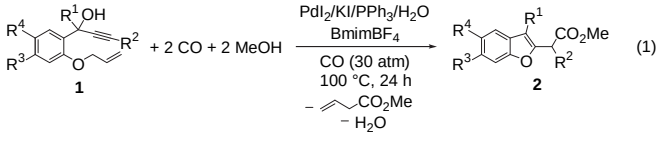


Scheme 2. Sequential homobimetallic catalysis leading to benzofuran-2-acetic esters **2**.



Scheme 3.

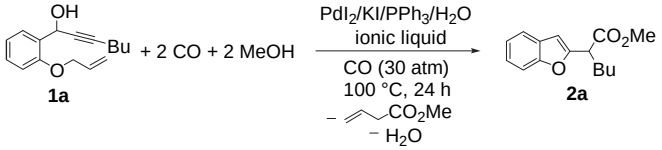
medium (Eq. 1), and that the solvent-catalytic system can be recycled several times without appreciable loss of catalytic activity. The possibility to employ an ionic liquid as the solvent for this reaction and to recycle the catalyst thus makes the process both more practical and attractive. In fact, the product can be easily separated from the palladium catalyst, by a simple extraction procedure. Even more importantly, particularly for a rather expensive metal, such as palladium, the catalyst recyclability allows for a significant increase of the ratio between the total amount of product obtained and the amount of catalyst employed with respect with the reaction carried out in conventional solvents.



(1)

The results obtained from the reaction of 1-(2-allyloxyphenyl) hept-2-yn-1-ol **1a** (R^1=R^3=R^4=H, R^2=Bu) (270 mg, 1 equiv) carried out in different ionic liquids as the solvent (3.75 mL) at 100 °C under 30 atm of CO for 24 h, in the presence of PdI_2 (4.0 mg, 1 mol %), KI (183 mg, 1 equiv), PPh_3 (11.5 mg, 4 mol %), H_2O (40 μL, 2 equiv), and MeOH (1.25 mL, 28 equiv) are shown in Table 1. As can be seen from the Table, the sequential catalytic process leading to the corresponding benzofuran derivative (2-benzofuran-2-ylhexanoic acid methyl ester, **2a**) took place in BmimCl, $BmimBF_4$, and $BmimNTf_2$ (Table 1, entries 1–3), even though with appreciable differences in the product yield, while it did not work in $BmimPF_6$ (Table 1, entry 4). The best yield of **2a** (84%) was obtained in $BmimBF_4$ (Table 1, entry 2), which was accordingly chosen as the reference solvent for the next experiments.

Table 1
Reactions of 1-(2-allyloxyphenyl)hept-2-yn-1-ol **1a** with CO in the presence of PdI_2–KI–PPh_3–H_2O–MeOH in different ionic liquids (ILs)[a]



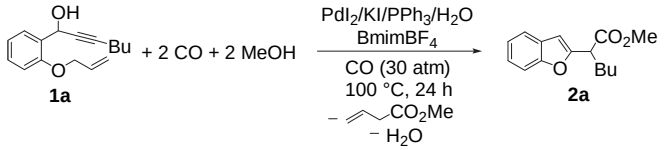
Entry	Solvent	Conversion of **1a** (%)[b]	Yield[c] of **2a** (%)
1	BmimCl	100	20
2	$BmimBF_4$	100	84
3	$BmimNTf_2$	99	65
4	$BmimPF_6$	0	—

[a] All reactions were carried out at 100 °C under 30 atm of CO for 24 h in the given ionic liquid as the solvent (3.75 mL), in the presence of PdI_2 (4.0 mg, 1 mol %), KI (183 mg, 1 equiv), PPh_3 (11.5 mg, 4 mol %), H_2O (40 μL, 2 equiv), **1a** (270.0 mg, 1 equiv), and MeOH (1.25 mL, 28 equiv). Conversion of **1a** was quantitative in all cases.
[b] Based on starting **1a**, by GLC analysis of the ethereal extract. See the Experimental section for details.
[c] Isolated yield based on starting **1a**.

The recyclability of the catalyst-solvent system was then assessed. The reaction crude was extracted several times with Et_2O, in order to separate the product, while a freshly prepared solution of **1a** (270 mg, 1 equiv) and H_2O (40 μL, 2 equiv) in MeOH (1.25 mL) was added to the ionic liquid phase. The resulting mixture was then allowed to react again under the usual conditions. The results obtained after six recycles, shown in Table 2 (entry 1), show that the catalytic activity of the ionic liquid phase slightly decreased after the first recycle, and then remained practically unchanged even after the sixth recycle. The decrease in yield of **2a** after the first run may be due to a partial deactivation of the catalytic system, which, however, after the second recycle, tended to maintain its activity quite constant. We refrain to propose a straightforward explanation for this behavior, which would require additional investigations. It is worth noting that it was not necessary to add PPh_3 after each recycle. In fact, when fresh PPh_3 was added, the results turned out to be less satisfactory, and lower yields of the product were obtained after the recycling procedure (Table 2, entries 2 and 3).

Having established the feasibility of the sequential homobimetallic catalytic process leading to **2a** in an ionic liquid, and the possibility to recycle to catalyst-solvent system, we then tested the reactivity of differently substituted substrates **1b**–**i** in order to verify the general applicability of the recyclable synthetic procedure. The results obtained using substrates bearing a π-donating or electron-withdrawing group on the ring, an aryl or sterically demanding substituent on the triple bond, or an additional substituent α to the hydroxyl group are shown in Table 3. As can be seen from the Table, the reaction worked nicely in all cases, thus

Table 2
Recyclable catalytic synthesis of 2-benzofuran-2-ylhexanoic acid methyl ester **2a** by Pd-catalyzed carbonylative heterocyclization of 1-(2-allyloxyphenyl)hept-2-yn-1-ol **1a** in $BmimBF_4$[a]



Entry	Mol % of PPh_4[b]	Run[c]	Yield[d] of **2aa** (%)
1	4	1	84
	—	2	68
	—	3	69
	—	4	68
	—	5	66
	—	6	66
	—	7	67
2	4	1	84
	1	2	63
	1	3	63
	1	4	62
	1	5	60
	1	6	60
	1	7	60
3	4	1	83
	4	2	63
	4	3	60
	4	4	60
	4	5	61
	4	6	62
	4	7	60

[a] All reactions were carried out at 100 °C under 30 atm of CO for 24 h in $BmimBF_4$ as the solvent, (3.75 mL) in the presence of PdI_2 (4.0 mg, 1 mol %), KI (183 mg, 1 equiv), PPh_3 (see footnote b), H_2O (40 μL, 2 equiv), **1a** (270.0 mg, 1 equiv) and MeOH (1.25 mL, 28 equiv). Conversion of **1a** was quantitative in all cases.
[b] Mol % of PPh_3 added in each run to the ionic liquid phase.
[c] Run 1 corresponds to the first experiment, the next runs to recycles. See text for details.
[d] Isolated yield based on starting **1a**.

allowing a general recyclable synthesis of benzofuran-2-acetic esters from readily available substrates.

3. Conclusion

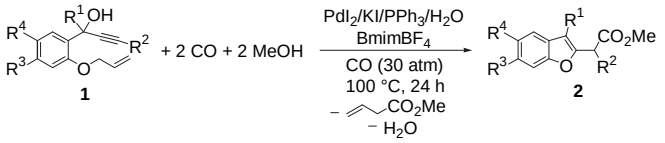
In conclusion, we have shown that the sequential homo-bimetallic catalytic process, consisting of Pd(0)-catalyzed deallylation followed by Pd(II)-catalyzed carbonylative heterocyclization, leading to benzofuran-2-acetic esters **2** from 1-(2-allyloxyphenyl)-2-yn-1-ols **1**, can be conveniently carried out in an ionic liquid, such as $BmimBF_4$, as the solvent. The use of $BmimBF_4$ allows both an easy removal of the product from the reaction mixture and the possibility to recycle the solvent-catalyst system several times without appreciable loss of catalytic activity. Benzofuran-2-acetic ester derivatives **2** are an important class of benzofuran derivatives,[3b,6–8] which are known to display interesting biological activities.[9] The present recyclable catalytic method represents an attractive, practical, and convenient approach for their production, starting from readily available starting materials.

4. Experimental section

4.1. General

Melting points were determined with a Reichert Thermovar apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded at 25 °C on a Bruker DPX Avance 300 spectrometer in $CDCl_3$ solutions at 300 MHz and 75 MHz, respectively, with Me_4Si as internal standard. IR spectra were taken with a Jasco FT-IR 4200

Table 3
Recyclable catalytic synthesis of benzofuran-2-acetic esters **2** by Pd-catalyzed carbonylative heterocyclization of 1-(2-allyloxyphenyl)-2-yn-1-ols **1** in $BmimBF_4$[a]



Entry	**1**	R^1	R^2	R^3	R^4	**2**	Run[b]	Yield[c] of **2** (%)
1	**1b**	Me	Bu	H	H	**2b**	1	84
							2	85
							3	85
							4	80
							5	86
							6	85
							7	88
2	**1c**	Ph	Bu	H	H	**2c**	1	84
							2	82
							3	82
							4	79
							5	83
							6	81
							7	82
3	**1d**	H	Ph	H	H	**2d**	1	66
							2	63
							3	64
							4	65
							5	66
							6	65
							7	65
4	**1e**	H	*t*-Bu	H	H	**2e**	1	76
							2	77
							3	80
							4	79
							5	73
							6	74
							7	73
5	**1f**	H	Bu	OMe	H	**2f**	1	80
							2	78
							3	81
							4	82
							5	79
							6	77
							7	80
6	**1g**	H	Bu	H	OMe	**2g**	1	76
							2	75
							3	79
							4	78
							5	70
							6	70
							7	72
7	**1h**	H	Bu	H	Cl	**2h**	1	85
							2	81
							3	78
							4	72
							5	77
							6	78
							7	81
8	**1i**	H	Ph	H	Cl	**2i**	1	80
							2	75
							3	76
							4	77
							5	74
							6	78
							7	79

[a] All reactions were carried out at 100 °C under 30 atm of CO for 24 h in $BmimBF_4$ as the solvent (3.75 mL), in the presence of PdI_2 (4.0 mg, 1 mol %), KI (183 mg, 1 equiv), PPh_3 (11.5 mg, 4 mol %), H_2O (40 μL, 2 equiv), **1** (1 equiv), and MeOH (1.25 mL, 28 equiv). Conversion of **1** was quantitative in all cases.
[b] Run 1 corresponds to the first experiment, the next runs to recycles. See text for details.
[c] Isolated yield based on starting **1**.

spectrometer. Mass spectra were obtained using a Shimadzu QP-2010 GC–MS apparatus at 70 eV ionization voltage. Microanalyses were carried out with a Carlo Erba Elemental Analyzer Mod. 1106. All reactions were analyzed by TLC on silica gel 60 F_{254} and by GLC using a Shimadzu GC-2010 gas chromatograph and capillary columns with polymethylsilicone +5% phenylsilicone as the stationary phase (HP-5). Column chromatography was performed on silica gel 60 (Merck, 70–230 mesh).

4.2. Preparation of substrates and ionic liquids

Substrates **1a**–**i** were prepared as we already described.[3] Ionic liquids BmimCl and $BmimBF_4$ were prepared as we already reported.[10] Ionic liquids $BmimNTf_2$[11] and BmimOTf[12] were prepared according to literature procedures.

4.3. General procedure for the synthesis of benzofuran-2-acetic esters 2 in ionic liquids (Tables 1–3)

A 35 mL stainless steel autoclave was charged with PdI_2 (4.0 mg, 1.1×10^{-2} mmol), KI (183 mg, 1.1 mmol), PPh_3 (11.5 mg, 4.4×10^{-2} mmol), and a solution of **1** (1.1 mmol) in anhydrous MeOH (1.25 mL, 30.8 mmol). The ionic liquid (3.75 mL) and H_2O (40 μL, 2.2 mmol) were then added, and the autoclave was sealed, purged at room temperature several times with CO with stirring (10 atm) and eventually pressurized at 30 atm. After stirring at 100 °C for 24 h, the autoclave was cooled and degassed. The mixture was then extracted with Et_2O (6×4 mL), and the residue (still containing the catalyst dissolved in the ionic liquid) was used as such for the next recycle (see below). The collected ethereal phases were concentrated and the product purified by column chromatography on silica gel to give pure benzofuran-2-acetic esters **2** (eluent: 1:1 hexane–CH_2Cl_2 for **2a**; 9:1 hexane–AcOEt for **2b**; 95:5 hexane–AcOEt for **2c**; 8:2 hexane–acetone for **2d** and **2i**; 8:2 hexane–AcOEt for **2e**, **2f**, and **2g**; 7:3 hexane–AcOEt for **2h**), whose characterization data agreed with those we already reported.[3] The isolated yields obtained in each experiment are given in Tables 1–3.

4.4. Recycling procedure (Tables 2 and 3)

After removal of Et_2O under vacuum, the residue obtained as described above, still containing the catalyst dissolved in the ionic liquid, was transferred into the autoclave. A solution of **1** (1.1 mmol) in anhydrous MeOH (1.25 mL, 30.8 mmol) and H_2O (40 μL, 2.2 mmol) was added, and then the same procedure described above was followed.

4.5. Characterization of products

*4.5.1. 2-Benzofuran-2-ylhexanoic acid methyl ester (**2a**).* Colorless oil. IR (film): 1743 (s), 1600 (w), 1585 (w), 1454 (m), 1252 (m), 1160 (m), 751 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.53–7.49 (1H, m, H-4 or H-7), 7.47–7.42 (1H, m, H-7 or H-4), 7.27–7.15 (2H, m, H-5+H-6), 6.59–6.58 (1H, m, H-3), 3.82 (1H, t, *J*=7.3 Hz, $CHCH_2$), 3.72 (3H, s, CO_2Me), 2.18–1.93 (2H, m, $CHCH_2$), 1.43–1.24 (4H, m, $CH_2CH_2CH_3$), 0.89 (3H, t, *J*=6.8 Hz, CH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.1, 155.3, 154.8, 128.4, 123.9, 122.7, 120.7, 111.1, 103.8, 52.3, 45.7, 30.6, 29.5, 22.4, 13.8. GC–MS (EI, 70 eV): *m*/*z* (%): 246 (33) [M^+], 190 (13), 189 (8), 187 (36), 145 (7), 144 (10), 132 (11), 131 (100), 115 (12). Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.41; H, 7.35.

*4.5.2. (3-Methylbenzofuran-2-yl)hexanoic acid methyl ester (**2b**).* Pale yellow oil. IR (film): 1743 (s), 1643 (w), 1613 (w), 1589 (w), 1455 (m), 1255 (m), 1246 (m), 1185 (m), 1167 (m), 747 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.47–7.40 (2H, m, H-4+H-7), 7.27–7.17 (2H, m, H-5+H-6), 3.84 (1H, dd, *J*=9.1, 6.6 Hz, $CHCH_2$), 3.68 (3H, s, CO_2Me), 2.21 (3H, s, $=CCH_3$), 2.23–1.96 (2H, m, $CHCH_2$) 1.41–1.17 (4H, m, $CH_2CH_2CH_3$), 0.87 (3H, t, *J*=7.1 Hz, CH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.1, 154.1, 149.6, 130.0, 123.8, 122.2, 119.0, 112.2, 111.1, 52.2, 43.6, 29.7, 29.5, 22.4, 13.9, 7.9. GC–MS (EI, 70 eV): *m*/*z* (%): 260 (23) [M^+], 203 (5), 202 (8), 201 (53), 171 (10), 158 (5), 157 (5), 146 (11), 145 (100), 131 (5), 128 (5), 115 (9). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found C, 73.76; H, 7.75.

*4.5.3. (3-Phenylbenzofuran-2-yl)hexanoic acid methyl ester (**2c**).* Pale yellow oil. IR (film): 1745 (s), 1611 (w), 1496 (w), 1454 (m), 1256 (m), 1215 (m), 1190 (m), 1167 (m), 1013 (w), 968 (w), 749 (m), 702 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.59–7.36 (7H, m, Ph+H-4+H-7), 7.34–7.20 (2H, m, H-5+H-6), 3.97 (1H, dd, *J*=9.0, 6.8 Hz, $CHCH_2$), 3.72 (3H, s, CO_2Me), 2.20–1.98 (2H, m, $CHCH_2$), 1.28–1.08 (4H, m, $CH_2CH_2CH_3$), 0.79 (3H, t, *J*=6.8 Hz, CH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.1, 154.3, 150.3, 132.0, 129.3, 128.9, 128.6, 127.6, 124.3, 122.8, 119.9, 119.6, 111.4, 52.3, 43.7, 30.0, 29.4, 22.3, 13.7. GC–MS (EI, 70 eV): *m*/*z* (%): 322 (70) [M^+], 264 (26), 263 (99), 219 (11), 208 (20), 207 (100), 205 (35), 179 (35), 178 (25), 165 (8). Anal. Calcd for $C_{21}H_{22}O_3$: C, 78.23; H, 6.88. Found C, 78.45; H, 6.86.

*4.5.4. Benzofuran-2-ylphenylacetic acid methyl ester (**2d**).* Yellow oil. IR (film): 1739 (s), 1600 (w), 1584 (w), 1453 (m), 1253 (m), 1199 (m), 1156 (s), 1010 (m), 751 (s), 723 (m), 699 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.50–7.26 (7H, m, Ph+H-4+H-7), 7.25–7.12 (2H, m, H-5+H-6), 6.57 (1H, t, *J*=1.0 Hz, H-3), 5.14 (1H, br s, *CH*Ph), 3.74 (3H, s, CO_2Me). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 155.0, 154.6, 128.8, 128.7, 128.2, 128.0, 124.1, 123.6, 122.7, 120.9, 111.1, 105.2, 52.6, 51.7. GC–MS (EI, 70 eV): *m*/*z* (%): 266 (20) [M^+], 208 (17), 207 (100), 179 (8), 178 (31), 176 (6), 152 (6), 89 (5). Anal. Calcd for $C_{17}H_{14}O_3$: C, 76.68; H, 5.30. Found C, 76.81; H, 5.29.

*4.5.5. 2-Benzofuran-2-yl-3,3-dimethylbutanoic acid methyl ester (**2e**).* Pale yellow solid, mp 60–61 °C. IR (KBr): 1733 (s), 1577 (w), 1474 (w), 1456 (m), 1435 (m), 1371 (m), 1321 (m), 1243 (m), 1205 (m), 1150 (s), 1043 (m), 1007 (m), 827 (m), 755 (m), 747 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.54–7.49 (1H, m, H-4 or H-7), 7.46–7.41 (1H, m, H-7 or H-4), 7.25–7.14 (2H, m, H-5+H-6), 6.74 (1H, dd, *J*=1.0, 0.3 Hz, H-3), 3.73 (1H, d, *J*=0.3 Hz, $CHCMe_3$), 3.69 (3H, s, CO_2Me), 1.08 (9H, s, CMe_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.2, 154.5, 153.9, 128.5, 123.7, 122.7, 120.7, 111.0, 105.5, 55.9, 51.7, 35.1, 28.0. GC–MS (EI, 70 eV): *m*/*z* (%): 246 (11) [M^+], 191 (12), 190 (100), 187 (8), 175 (22), 158 (35), 131 (27), 130 (9), 102 (8), 57 (30). Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found C, 73.02; H, 7.38.

*4.5.6. 2-(6-Methoxybenzofuran-2-yl)hexanoic acid methyl ester (**2f**).* Yellow oil. IR (film): 1741 (s), 1624 (m), 1587 (w), 1492 (m), 1438 (m), 1293 (m), 1274 (m), 1195 (m), 1149 (m), 1107 (m), 1027 (m), 961 (w), 823 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.35 (1H, d, *J*=8.6 Hz, H-4), 6.99 (1H, d, *J*=2.2 Hz, H-7), 6.83 (1H, dd, *J*=8.6, 2.2 Hz, H-5), 6.50 (1H, s, H-3), 3.83–3.75 (1H, m, *CH*Bu), 3.81 (3H, s, $ArOCH_3$), 3.71 (3H, s, CO_2Me), 2.15–1.90 (2H, m, $CHCH_2$), 1.43–1.25 (4H, m, $CH_2CH_2CH_3$), 0.89 (3H, t, *J*=6.9 Hz, CH_2CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.3, 157.8, 155.7, 154.3, 121.7, 120.8, 111.7, 103.5, 96.0, 55.7, 52.2, 45.7, 30.5, 29.5, 22.4, 13.9. GC–MS (EI, 70 eV): *m*/*z* (%): 276 (54) [M^+], 219 (33), 218 (15), 217 (95), 174 (8), 162 (12), 161 (100), 159 (16). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found C, 69.45; H, 7.30.

*4.5.7. 2-(5-Methoxybenzofuran-2-yl)hexanoic acid methyl ester (**2g**).* Yellow oil. IR (film): 1741 (s), 1615 (w), 1602 (w), 1477 (m), 1447 (m), 1435 (m), 1205 (m), 1167 (m), 1031 (w) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.32 (1H, dt, *J*=8.8, 0.7 Hz, H-7), 6.98–6.96 (1H, m, H-4), 6.84 (1H, dd, *J*=8.8, 2.7 Hz, H-6), 6.52 (1H, t, *J*=0.7 Hz, H-3), 3.82–3.76 (1H, m, *CH*Bu), 3.80 (3H, s, $ArOCH_3$), 3.71 (3H, s, CO_2Me),

2.16–1.91 (2H, m, CHCH_2), 1.43–1.24 (4H, m, CH_2CH_2CH$_3$), 0.89 (3H, t, J=6.9 Hz, CH$_2$CH_3). ^{13}C NMR (75 MHz, CDCl$_3$): δ 172.1, 156.1, 156.0, 149.8, 129.0, 112.5, 111.5, 103.9, 103.4, 55.9, 52.3, 45.8, 30.6, 29.5, 22.4, 13.9. GC–MS (EI, 70 eV): m/z (%): 276 (33) [M$^+$], 220 (12), 219 (10), 218 (7), 217 (43), 216 (6), 191 (6), 162 (12), 161 (100). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.54; H, 7.30. Found C, 69.69; H, 7.29.

*4.5.8. 2-(5-Chlorobenzofuran-2-yl)hexanoic acid methyl ester (**2h**).* Yellow oil. IR (film): 1742 (s), 1594 (w), 1447 (m), 1259 (m), 1159 (m), 1061 (w), 801 (m), 696 (w) cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.46 (1H, dt, J=2.0, 0.7 Hz, H-4), 7.34 (1H, dt, J=8.6, 0.7 Hz, H-7), 7.18 (1H, dd, J=8.6, 2.0 Hz, H-6), 6.54 (1H, t, J=0.7 Hz, H-3), 3.81 (1H, t, J=7.6 Hz, C*H*Bu), 3.72 (3H, s, CO$_2$Me), 2.17–1.91 (2H, m, CHCH_2), 1.43–1.24 (4H, m, CH_2CH_2CH$_3$), 0.89 (3H, t, J=7.0 Hz, CH$_2$CH_3). ^{13}C NMR (75 MHz, CDCl$_3$): δ 171.8, 157.0, 153.1, 129.8, 128.3, 124.1, 120.3, 112.1, 103.5, 52.4, 45.7, 30.5, 29.5, 22.4, 13.8. GC–MS (EI, 70 eV): m/z (%): 282 (7) [(M+2)$^+$], 280 (22) [M$^+$], 224 (17), 223 (15), 221 (34), 167 (33), 166 (11), 165 (100), 115 (12). Anal. Calcd for $C_{15}H_{17}ClO_3$: C, 64.17; H, 6.10; Cl, 12.63. Found C, 64.26; H, 6.08; Cl, 12.61.

*4.5.9. (5-Chlorobenzofuran-2-yl)phenylacetic acid methyl ester (**2i**).* Yellow oil. IR (film): 1743 (s), 1593 (m), 1446 (m), 1259 (m), 1199 (m), 1153 (s), 1060 (w), 1010 (m), 801 (m), 723 (m), 695 (m) cm^{-1}. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.45–7.26 (7H, m, Ph+H-4+H-7), 7.16 (1H, dd, J=8.8, 2.2 Hz, H-6), 6.52 (1H, t, J=1.0 Hz, H-3), 5.11 (1H, br s, C*H*Ph), 3.74 (3H, s, CO$_2$Me). ^{13}C NMR (75 MHz, CDCl$_3$): δ 170.3, 156.2, 153.3, 135.1, 129.6, 128.9, 128.6, 128.3, 128.2, 124.3, 120.5, 112.1, 104.9, 52.7, 51.6. GC–MS (EI, 70 eV): m/z (%): 302 (9) [(M+2)$^+$], 300 (26) [M$^+$], 243 (43), 242 (21), 241 (100), 206 (10), 205 (13), 178 (38), 176 (14). Anal. Calcd for $C_{17}H_{13}ClO_3$: C, 67.89; H, 4.36, Cl, 11.79. Found C, 67.95; H, 4.35; Cl, 11.77.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.05.109. These data include MOL files and InChiKeys of the most important compounds described in this article.

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